

AMENDMENTS

In the Claims:

Please amend the claim as set out below.

1. (Currently Amended) A transgenic mouse comprising a polynucleotide encoding a human C5aR or humanized C5aR, wherein the C5a endogenous to the mouse binds to and effects signalling of the human or humanized C5aR, wherein said signalling is capable of inducing arthritis upon administration of sera from arthritic K/BxN mice, and wherein the transgenic mouse is homozygous for the polynucleotide encoding a human or humanized C5aR and wherein the endogenous C5aR coding sequences are disrupted.

2. (Previously Presented) The transgenic mouse according to claim 1, wherein the polynucleotide encodes human C5aR comprising the amino acid sequence as shown in SEQ ID NO:3, or an allelic variant thereof.

3. (Previously Presented) The transgenic mouse according to claim 1, wherein the polynucleotide comprises the nucleotide sequence as shown in SEQ ID NO:2, or an allelic variant thereof.

4. (Previously Presented) The transgenic mouse according to claim 1, wherein the polynucleotide encodes humanized C5aR.

5. (Previously Presented) The transgenic mouse according to claim 4, wherein the humanized C5aR comprises a C5aR sequence endogenous to the mouse wherein at least one extracellular or intracellular domain is replaced with the corresponding human C5aR domain.

6. - 9. (Cancelled)

10. (Currently Amended) The transgenic mouse according to claim 1, wherein the endogenous C5aR coding sequences, ~~or fragments thereof~~, have been replaced with a corresponding human C5aR coding sequence ~~or fragment thereof~~.

11. – 13. (Cancelled)

14. (Previously Presented) An isolated cell(s), cell line, tissue or organ obtained from the transgenic mouse of claim 1, the isolated cell, cell line, tissue or organ comprising a polynucleotide encoding a human C5aR or humanized C5aR.

15. (Currently Amended) A method for producing a transgenic mouse for testing compounds for an effect on a phenotype associated with C5aR signalling, the method comprising:

introducing into the genome of a mouse a polynucleotide construct encoding human C5aR, humanized C5aR or a fragment of human C5aR[[.]] to produce a transgenic mouse, wherein the C5a endogenous to the mouse binds to and effects signalling of the human or humanized C5aR, wherein said signalling is capable of inducing arthritis upon administration of sera from arthritic K/BxN mice, and wherein the endogenous C5aR coding sequences are disrupted.

16. (Previously Presented) The method according to claim 15, wherein the polynucleotide construct encodes human C5aR.

17. (Previously Presented) The method according to claim 16, wherein the polynucleotide construct encodes a polypeptide comprising the amino acid sequence as shown in SEQ ID NO:3, or an allelic variant thereof.

18. (Previously Presented) The method according to claim 16, wherein the polynucleotide construct comprises the nucleotide sequence as shown in SEQ ID NO:2, or an allelic variant thereof.

19. (Previously Presented) The method according to claim 15, wherein the polynucleotide construct encodes humanized C5aR.

20. (Previously Presented) The method according to claim 15, wherein the polynucleotide construct encodes a fragment of human C5aR.

21. (Cancelled)

22. (Previously Presented) The method according to claim 20, wherein the fragment encompasses at least one extracellular domain of human C5aR.

23. - 26 (Cancelled)

27. (Currently Amended) The method according to claim 15, wherein the method comprises replacing the endogenous C5aR coding sequences, ~~or fragments thereof~~, with a corresponding human C5aR coding sequence or fragment thereof.

28. (Currently Amended) A method for screening evaluating at least one pharmacokinetic and/or pharmacodynamic effect of a candidate compound for anti-inflammatory activity in the transgenic mouse according to claim 1, or isolated tissue or cells obtained therefrom, the method comprising:

administering a candidate compound to [[a]] the transgenic mouse, according to claim 1 or isolated tissue or cells obtained therefrom, wherein an inflammatory response is induced in the transgenic mouse by administration of sera from arthritic K/BxN mice; and

examining an at least one pharmacokinetic and/or pharmacodynamic effect of the candidate compound on the inflammatory response in the transgenic mouse or isolated tissue or cells obtained therefrom;

wherein a decrease in the inflammatory response in the transgenic mouse, or isolated tissue or cells obtained therefrom, as compared to the inflammatory response in the absence of the candidate compound, indicates the candidate compound has anti-inflammatory activity.

29. – 39. (Cancelled)

40. (Currently Amended) The method according to claim 28 wherein the candidate compound is selected from the group consisting of: a peptide, including a peptide derived from C5aR or C5a or other

non-C5aR peptide and capable of inhibiting, reducing or repressing a C5aR function, a C5aR dominant-negative mutant; a non peptide inhibitor of C5aR; an antibody or antibody fragment which binds to C5aR and inhibits a C5aR function; a small organic molecule, a nucleic acid encoding said peptide derived from C5aR or C5a or other non-C5aR peptide inhibitor, an antisense nucleic acid directed against C5aR-encoding mRNA, an anti-C5aR ribozyme, and a small interfering RNA (RNAi) that targets C5aR gene expression.

41. (Cancelled)